OCULAR TECHNOLOGY GROUP - *International*

REFITTING BIOFINITY® MULTIFOCAL CONTACT LENS WEARERS WITH MYDAY® MULTIFOCAL CONTACT LENSES

CLINICAL INVESTIGATIONAL PLAN

Sponsor:	CooperVision International Limited (CVIL)
Study Sponsor Number:	EX-MKTG-155
OTG-*i* Study Number:	ID23-62
IRAS Project ID:	338011
Version:	1.0
Issue Date:	11th December 2023

[redacted]

[redacted]

Clinical Investigational Plan

Refitting Biofinity® Multifocal Contact Lenses Wearers with MyDay® Multifocal Contact Lenses

OTG-i Study Number and Version: ID23-62 Version 1.0

Study Sponsor Number: EX-MKTG-155

Issue Date: 11th December 2023

Protocol Signature Page

As Chief Investigator, I agree to conduct this study in accordance with all applicable laws and regulations and in compliance with the provisions of this Clinical Investigational Plan.

I am responsible for ensuring that the investigation is conducted according to this plan and for protecting the rights, safety, and welfare of the research participants.

[redacted]

Confidentiality Statement

The information in the following document is provided to you as an investigator, potential investigator, or consultant, for review by you, your staff, and applicable Ethics Committee or Institutional Review Board, and is considered confidential. It is understood that the information will not be disclosed to others without written authorization from OCULAR TECHNOLOGY GROUP - *International*, except to the extent necessary to obtain informed consent from the study participants.

DOCUMENT CHANGE HISTORY

Revision	Originator	Description of Change(s)	Date

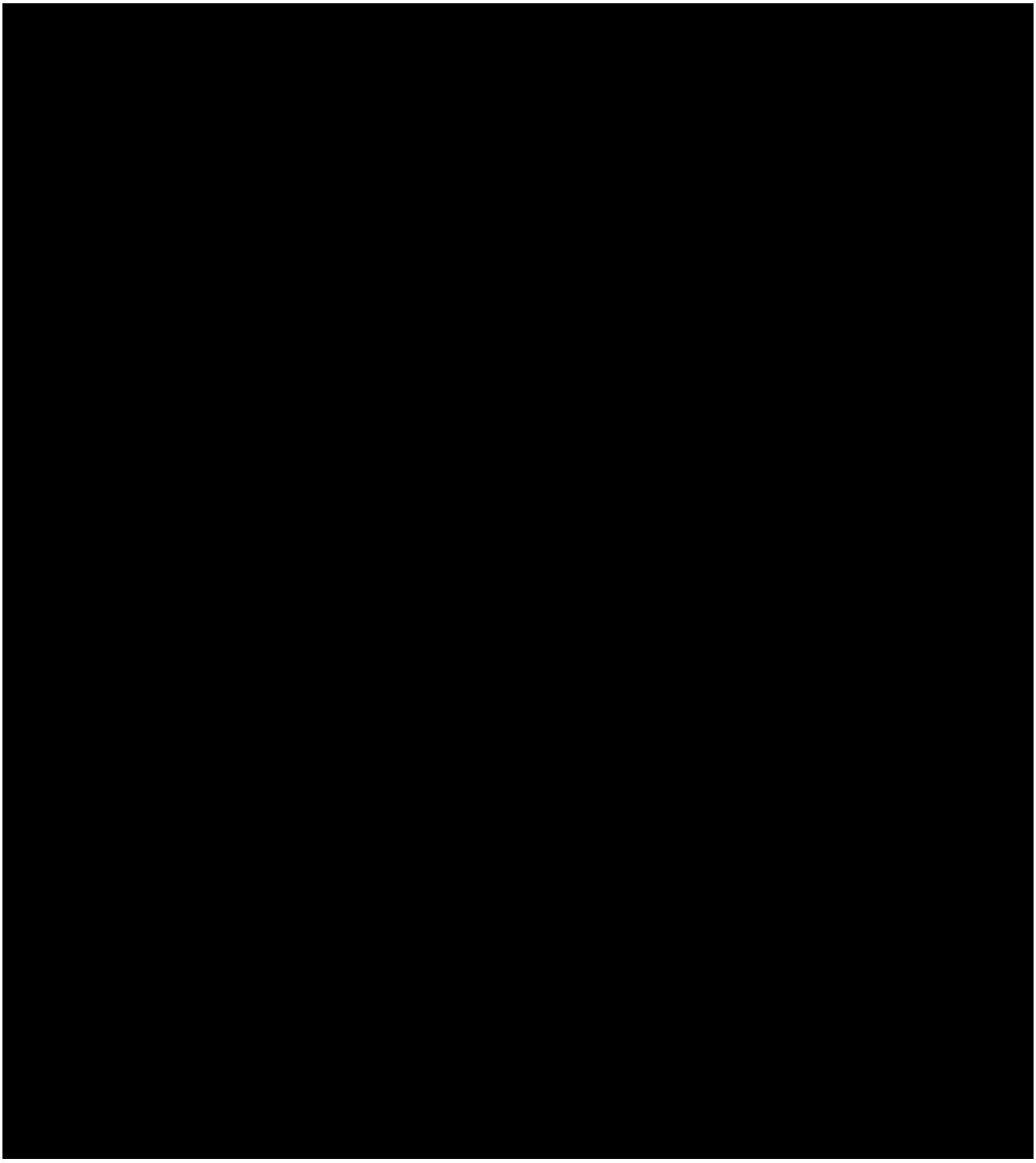

Table of Contents

1 OVERALL SYNOPSIS 8
2 INTRODUCTION AND RATIONALE 11
2.1 Background 11
2.2 Objective 11
2.3 Hypotheses 11
2.4 Endpoints 11
3 STUDY SPONSOR AND INVESTIGATORS 12
3.1 Study Sponsor 12
3.2 Clinical Research Organisation 12
3.3 Study Site & Investigators 12
3.4 Medical Monitor 12
3.5 Data Controller and Statistical Analysis 12
3.6 Independent Ethics Committee 12
4 STUDY MATERIAL 13
4.1 Reference Contact Lenses 13
4.2 Test Contact Lenses 13
5 STUDY POPULATION 14
5.1 Recruitment Procedure 14
5.2 Number of Participants 14
5.3 Inclusion and Exclusion Criteria 14
5.3.1 INCLUSION CRITERIA 14
5.3.2 EXCLUSION CRITERIA 15
5.4 Premature Withdrawal 15
5.5 Informed Consent 16
6 STUDY DESIGN & PROCEDURES 16
6.1 Experimental Design 16
6.2 Experimental Routine 17
6.3 End of Study 18
6.4 Participant Instruction 18
6.5 Procedures 18
6.5.1 EFFICACY PROCEDURES 18
6.5.2 [redacted]
6.5.3 POPULATION PROFILING PROCEDURES 19

6.5.4 STUDY MANAGEMENT PROCEDURES 19
6.6 Study Visit Routine 19
6.6.1 VISIT 1 – SCREENING ENROLMENT FITTING DISPENSING VISIT 19
▪ BIOFINITY® MULTIFOCAL REMOVE INITIAL CONTACT LENS & INSERT BIOFINITY® MULTIFOCAL SECOND CONTACT LENS AND WEAR FOR 10 MINUTES 20
6.6.2 VISIT 2 – BIOFINITY® MULTIFOCAL CONTACT LENS FOLLOW-UP & MYDAY® MULTIFOCAL CONTACT LENS FITTING AND DISPENSING VISIT (14 ± 3 DAYS AFTER VISIT 1) 20
▪ MYDAY® MULTIFOCAL REMOVE INITIAL CONTACT LENS & INSERT MYDAY® MULTIFOCAL SECOND CONTACT LENS AND WEAR FOR 10 MINUTES 20
6.6.3 VISIT 3– MYDAY® MULTIFOCAL CONTACT LENS FOLLOW-UP & DISCHARGE VISIT (14 ± 3 DAYS AFTER VISIT 2) 21
7 SAMPLE SIZE DETERMINATION AND STATISTICAL ANALYSIS 21
7.1 Sample Size Determination 21
7.2 Statistical Analysis Plan 21
8 RISK ANALYSIS 22
8.1 Benefits 22
8.2 Risks 22
8.3 Conclusion 22
9 ADVERSE EVENTS AND REPORTING 22
9.1 Adverse Events 22
9.1.1 ADVERSE EVENT DEFINITIONS 23
9.1.2 NORMAL OR ADAPTIVE SYMPTOMS 24
9.1.3 PROCEDURES FOR ADVERSE EVENTS 24
9.2 Reporting Adverse Events 25
10 DEVICE DEFICIENCIES 25
11 INVESTIGATOR, SPONSOR AND MEDICAL MONITOR RESPONSIBILITIES 26
11.1 Investigator Responsibilities 26
11.2 Sponsor Responsibilities 26
11.3 Medical Monitor Responsibilities 27
12 GENERAL CLINICAL MANAGEMENT 27
12.1 Data Recording 27
12.2 Clinical Monitoring 27
12.3 Study Product Accounting 27
12.4 Participant Compliance Monitoring 28

12.5 [redacted]

13 ADMINISTRATIVE MANAGEMENT 28

13.1 Relevant Standards 28

13.2 Deviations from the Protocol 29

13.2.1 GENERAL 29

13.2.2 MAJOR PROTOCOL DEVIATIONS 29

13.2.3 MINOR PROTOCOL DEVIATIONS 29

13.3 Modifications to the Clinical Investigational Plan 29

13.4 Termination of the Study 30

13.5 Data Protection 30

13.6 Data Handling and Record Keeping 30

13.7 Reporting 30

13.8 Publication Policy 30

13.9 [redacted]

13.10 Indemnity / Insurance 30

14 [redacted]

15 [redacted]

1 OVERALL SYNOPSIS

Study Sponsor	The Sponsor for this investigation will be CooperVision International Limited (CVIL) Delta Park, Concorde Way, Segensworth North, Fareham PO15 5RL, UK. The sponsor contact will be Dr Jose Vega.
Title of Study	Refitting Biofinity multifocal contact lens wearer with MyDay multifocal contact lenses.
Protocol Number	EX-MKTG-155 ID23-62
Type of study	The study will be conducted following an interventional, prospective, open label, sequential study design.
Study Population	Required: 60 completed participants as per protocol (cohort) with a minimum of 66 to be enrolled. Planned: Up to 70 screened, with the aim of enrolling 66 participants.
Duration of study treatment	14 (-0/+3) days of daily disposable, daily contact lens wear per study contact lens type.
Inclusion Criteria	In order to be enrolled, each participant shall meet the following criteria: i. Age 40 years and older; ii. Current multifocal contact lens wearer (other than MyDay® multifocal but can include Biofinity® multifocal); iii. Spectacle refraction: Distance: Sphere: -6.00D to + 4.00D Astigmatism: 0.00D to -0.75D Near Addition: +0.75D to +2.50D iv. Best corrected visual acuity of at least 20/25 in each eye. The prospective participants will be given a Participant Information Sheet to read and an Informed Consent Form to sign prior to any evaluation.
Exclusion Criteria	The following are specific criteria that exclude a candidate from enrolment in this study: i. Acute and subacute inflammation or infection of the anterior chamber of the eye. ii. Any eye disease, injury or abnormality that affects the cornea, conjunctiva or eyelids that would contraindicate contact lens wear; iii. Corneal hypoesthesia (reduced corneal sensitivity), if not aphakic iv. Severe insufficiency of lacrimal secretion (dry eyes). v. Any systemic disease that may affect the eye or may be exaggerated by wearing contact lenses (e.g. acne and eczema). vi. Allergic reactions of ocular surfaces or adnexa that may be induced or exaggerated by wearing contact lenses or use of contact lens solutions vii. Any active corneal infection (bacterial, fungal, protozoal or viral). viii. Newly prescribed (within the past 30 days) use of some systemic medications (such as antihistamines, decongestants, diuretics, muscle relaxants, tranquilizers, stimulants, anti-depressants, anti-psychotics, oral contraceptives) or new prescription eyedrops which is not rewetting/lubricating eyedrops for which contact lens wear could be contraindicated as determined by the investigator; ix. Monocular participants (only one eye with functional vision) or participants fit with only one contact lens;

	x. Subjects with slit lamp findings greater than grade 1 (e.g. edema, infiltrates, corneal neovascularization, corneal staining, tarsal abnormalities, conjunctival, anterior segment inflammation) as per ISO 11980, any previous history or signs of a contact lens related corneal inflammatory event (past corneal ulcers), or any other ocular abnormality that may contraindicate contact lens wear at the enrolment visit; xi. History of corneal refractive surgery xii. Enrolment of the family members of the investigator, family members of the investigator's staff, or individuals living in the households of these individuals. xiii. Current wearer of the test contact lens MyDay® multifocal contact lens.
Planned Start Date	January 2023
Overall Study Duration	Nine months. This includes the study enrolment period, active contact lens wear period of approximately three months and study close out.
Objectives	The primary objective of the study will be to assess handling characteristics (insertion and removal). The secondary objectives will be to measure logMAR visual acuity. [redacted]
[redacted]	[redacted]
Efficacy Endpoints	The primary efficacy endpoints will be ease of handling over the week preceding the follow-up visit, calculated as the ease of insertion and ease of removal. The secondary endpoint will be mean logMAR visual acuity calculated as the mean of distance, intermediate and near logMAR visual acuities.
[redacted]	[redacted]
[redacted]	[redacted]

<table>
<tr><td></td><td colspan="3">[redacted]</td></tr>
<tr><td>[redacted]</td><td colspan="3">[redacted]</td></tr>
<tr><td>Population Profiling Procedures</td><td colspan="3">The procedures to profile the population key characteristics will be:
i. Demographics and medical & ocular history (including concomitant treatment) questionnaires;
ii. [redacted]</td></tr>
<tr><td></td><td>☐ Single masked (participant)
☐ Single masked (investigator)
☐ Double masked*
☐ Sponsor masked
☒ Open label</td><td colspan="2">☒ Single group
☐ Parallel group
☐ Crossover
☐ Contralateral</td></tr>
<tr><td>Reference Product</td><td colspan="3">The reference contact lenses will be Biofinity® multifocal CE marked and currently marketed in the UK planned replacement contact lenses that can worn up to 30 days of daily wear. The reference contact lenses will be used as per their CE marking.</td></tr>
<tr><td>Test Products</td><td colspan="3">The test contact lenses will be MyDay® multifocal CE marked daily disposable contact lenses currently marketed in the UK. The test contact lenses will be used as per their CE marking.</td></tr>
<tr><td>Study Visits</td><td colspan="3">The participants will attend a total of three visits over on average a four-week period (maximum five weeks).
The visit schedule will be as follow:
Visit 1 Screening/ enrolment / fitting & dispensing of Biofinity® multifocal contact lens visit.
Visit 2 Biofinity® multifocal contact lens follow-up & MyDay® multifocal contact lens fitting and dispensing visit (14 ± 3 days after Visit 1).
Visit 3 MyDay® multifocal contact lens follow-up & discharge visit (14 ± 3 days after Visit 2).</td></tr>
<tr><td>Keywords</td><td colspan="3">Biofinity ® multifocal, MyDay® multifocal, Refitting.</td></tr>
<tr><td>Regulatory Status</td><td colspan="3">The study requires Ethics Committee (EC) approval prior to initiation.</td></tr>
<tr><td rowspan="2">Responsibilities</td><td>Sponsor</td><td colspan="2">Name: CooperVision International Limited (CVIL)
[redacted]</td></tr>
<tr><td>CRO and Data Management</td><td colspan="2">OCULAR TECHNOLOGY GROUP - *International*
[redacted]</td></tr>
</table>

2 INTRODUCTION AND RATIONALE

2.1 Background

Biofinity® multifocal contact lenses and MyDay® multifocal contact lenses are two successful contact lenses to correct presbyopia currently CE marked and on the UK market. Biofinity® multifocal contact lenses fitting is based upon the selection of the optimal contact lens from the choice of eight different near additions. MyDay® multifocal a more recently developed contact lens only uses three near addition designs to fit the same population of presbyopes. The simpler fitting system results in less chair time for both the eyecare practitioner and the patient. A very large number of presbyopes are currently successfully wearing Biofinity® multifocal contact lenses, the question is therefore to understand if wearers who have successfully adapted to wearing Biofinity® multifocal contact lenses could also be successful wearers of MyDay® multifocal.

[redacted]

2.2 Objective

The primary objective of the study will be to assess handling characteristics (insertion and removal).
The secondary objectives will be to measure logMAR visual acuity.

[redacted]

2.3 Hypotheses

The primary hypothesis is that the ease of handling (EOH) at both insertion and removal of the test contact lens is non-inferior to the reference contact lens.

[redacted]

The secondary hypothesis is that high luminance, high contrast logMAR visual acuity at Distance, Intermediate and Near (logMAR ^{DIN}) of the test contact lens is non-inferior to control contact lens.

[redacted]

2.4 Endpoints

The primary efficacy endpoints will be ease of handling over the week preceding the follow-up visit, calculated as the ease of insertion and ease of removal.

The secondary endpoint will be mean logMAR visual acuity calculated as the mean of distance, intermediate and near logMAR visual acuities.

[redacted]

3 STUDY SPONSOR AND INVESTIGATORS

3.1 Study Sponsor

The Sponsor for this investigation will be CooperVision International Limited (CVIL) Delta Park, Concorde Way, Segensworth North, Fareham PO15 5RL, UK. The sponsor contact will be Dr Jose Vega.

3.2 Clinical Research Organisation

The Clinical Research Organisation (CRO) will be OCULAR TECHNOLOGY GROUP - *International* (OTG-*i*) at: Lower Ground Floor, 66 Buckingham Gate, London. SW1E 6AU. United Kingdom.

The study director will be Dr Michel Guillon, PhD, FCOptom, FAAO, FBCLA, CPI Lower Ground Floor, 66 Buckingham Gate, London SW1E 6AU. United Kingdom.

3.3 Study Site & Investigators

The study site will be OCULAR TECHNOLOGY GROUP - International (OTG-i) Clinic at Lower Ground Floor, 66 Buckingham Gate, London SW1E 6AU. United Kingdom.

The study Principal Investigator (PI) will be Dr Michel Guillon, PhD, FCOptom, FAAO, BCLA, CPI, and the co-investigators [redacted].

3.4 Medical Monitor

The medical monitor at the OTG-*i* Research Clinic [redacted]; the medical monitor is contracted to OTG-*i* Research Clinic for this activity.

3.5 Data Controller and Statistical Analysis

The data controller [redacted] OCULAR TECHNOLOGY GROUP – *International*. The statistical analysis design and statistical analysis will be the responsibility [redacted] OCULAR TECHNOLOGY GROUP – *International*.

3.6 Independent Ethics Committee

Before clinical study initiation, this protocol, information given to participants (PIS), the informed consent (ICF) forms and any advertisements planned for participant recruitment will be submitted to an Independent Ethics Committee (IEC) for approval. The IEC will be provided with all information as required by local regulations and/or the IEC. At the end of the study, the Investigator will notify the IEC about the study's completion. The IEC also will be notified if the study is terminated prematurely. Finally, the Investigator will report to the IEC on the progress of the study at intervals stipulated by the IEC.

The study will be submitted to the Integrated Research Application System (IRAS) centralised National Research Ethics Service for review. The investigation will not start until the no objection notification has been received.

The Investigator will provide documentation of the IEC approval to the sponsor. The approval will be dated and will identify the applicable protocol, amendments (if any), informed consent form, all applicable recruiting materials, written information for participants, and participant compensation programs.

4 STUDY MATERIAL

4.1 Reference Contact Lenses

The reference contact lenses will be Biofinity® multifocal CE marked and currently marketed in the UK planned replacement contact lenses that can worn up to 30 days of daily wear. The reference contact lenses will be used as per their CE marking. Details of the material properties and contact lens design are given in Table 1A.

Table 1A – Reference Contact Lenses

	Biofinity® multifocal
Manufacturer	CooperVision Inc.
USAN material name	Comfilcon A
Water content	48%
Oxygen Permeability	142 Dk/t (at -3.00D)
Diameter (mm)	14.0mm
Base curve (mm)	8.6mm
Power (D)	6.00D to -8.00D (0.50D steps after -6.00D)
Add power	+1.00, +1.50. +2.00. +2.50
Lens Design	Multifocal / Balanced Progressive™ Technology
Indications	Daily wear soft contact lens

The contact lenses will be worn on a daily disposable modality, that is the contact lenses will be worn during the day, removed and discarded at the end of each day before sleep, a similar new pair of contact lenses being used each day as per the user instructions [redacted]

4.2 Test Contact Lenses

The test contact lenses will be MyDay® multifocal CE marked and currently marketed in the UK daily disposable contact lenses. The test contact lenses will be used as per their CE marking. Details of the material properties and contact lens design are given in Table 1B.

Table 1B – Test Contact Lenses

	MyDay® multifocal
Manufacturer	CooperVision Inc.
USAN material name	stenfilcon A
Water content	54%
Oxygen Permeability	80 x 10^{-11} (cm^2/sec) x (ml O_2)/(ml x mm Hg)
Diameter (mm)	14.2mm
Base curve (mm)	8.4mm
Power (D)	
Distance	+4.00 to -6.00D in 0.25 steps
Near Add	Low, medium and high

Lens Design	Multifocal / Binocular Progressive System™
Indications	Daily wear soft contact lens

The contact lenses will be worn on a daily disposable modality, that is the contact lenses will be worn during the day, removed and discarded at the end of each day before sleep, a similar new pair of contact lenses being used each day as per the user instructions [redacted]

5 STUDY POPULATION

5.1 Recruitment Procedure

The prospective participants will be selected from the existing clinical population of the OCULAR TECHNOLOGY GROUP- *International* clinic. The participants fulfilling the criteria for inclusion and none of the exclusion criteria will be invited in a random fashion to participate in the study until the study population is achieved. In addition, the study will be advertised in social media and / or the local press to help with recruitment.

The prospective participants from OCULAR TECHNOLOGY GROUP- *International* will initially be contacted by e-mail and if they indicate they are interested in taking part, the investigation will be explained in detail by telephone; if they then confirm their interest, a screening / enrolment / dispensing visit will be scheduled. A copy of the Participant Information Sheet [redacted] and Informed Consent [redacted] will be sent to the prospective participants for information at least 24 hours prior to the visit.

The prospective participants responding to the approved advertisement by contacting the clinic via e-mail or telephone and indicating that they are interested in taking part, will be explained the study in detail by telephone; if they then confirm their interest a screening / enrolment / dispensing visit will be scheduled. A copy of the Participant Information Sheet and Informed Consent will be sent to the prospective participants for information at least 24 hours prior to the enrolment visit.

The prospective participants will be given a Participant Information Sheet to read and an Informed Consent to sign prior to any evaluation.

5.2 Number of Participants

Up to 70 participants to be screened, with the aim to enrol up to 66 participants and with a view to achieve a cohort (participants completing the study as per protocol) sample size of 60 made up of approximately 20 in each of the low (near addition +0.75D to +1.25D), medium (near addition +1.50D and +1.75D) or high (near addition+2.00D to +2.50D) spectacle additions groups. Therefore 66 participants will be enrolled to account for drop out based upon a potential 10% drop out rate, has been determined to be optimal, balancing the need for sufficient discrimination and limiting inconvenience to participants by not inflating the study sample (see section 7.1).

5.3 Inclusion and Exclusion Criteria

5.3.1 INCLUSION CRITERIA

In order to be enrolled, each participant shall meet the following criteria:

i. Age 40 years and older
ii. Current multifocal contact lens wearer (other than MyDay® multifocal but can include Biofinity® multifocal);
iii. Spectacle refraction:

Distance:	Sphere: -6.00D to + 4.00D	
Astigmatism:	0.00D to -0.75D	
Near Addition:	Low	+0.75D to +1.25D
	Medium	+1.50D and +1.75D
	High	+2.00D to +2.50D

iv. Best corrected visual acuity of at least 20/25 in each eye.

The prospective participants will be given a Participant Information Sheet to read and an Informed Consent Form to sign prior to any evaluation.

5.3.2 EXCLUSION CRITERIA

To be eligible as a participant, each candidate shall be free of any ocular or medical condition that may affect the results of this study.

The following are specific criteria that exclude a candidate from enrolment in this study:

i. Acute and subacute inflammation or infection of the anterior chamber of the eye.
ii. Any eye disease, injury or abnormality that affects the cornea, conjunctiva or eyelids that would contraindicate contact lens wear;
iii. Corneal hypoesthesia (reduced corneal sensitivity), if not aphakic
iv. Severe insufficiency of lacrimal secretion (dry eyes).
v. Any systemic disease that may affect the eye or may be exaggerated by wearing contact lenses (e.g. acne and eczema).
vi. Allergic reactions of ocular surfaces or adnexa that may be induced or exaggerated by wearing contact lenses or use of contact lens solutions
vii. Any active corneal infection (bacterial, fungal, protozoal or viral).
viii. Newly prescribed (within the past 30 days) use of some systemic medications (such as antihistamines, decongestants, diuretics, muscle relaxants, tranquilizers, stimulants, anti-depressants, anti-psychotics, oral contraceptives) or new prescription eyedrops which is not rewetting/lubricating eyedrops for which contact lens wear could be contraindicated as determined by the investigator;
ix. Monocular participants (only one eye with functional vision) or participants fit with only one contact lens;
x. Subjects with slit lamp findings greater than grade 1 (e.g. edema, infiltrates, corneal neovascularization, corneal staining, tarsal abnormalities, conjunctival, anterior segment inflammation) as per ISO 11980, any previous history or signs of a contact lens related corneal inflammatory event (past corneal ulcers), or any other ocular abnormality that may contraindicate contact lens wear at the enrolment visit;
xi. History of corneal refractive surgery
xii. Enrolment of the family members of the investigator, family members of the investigator's staff, or individuals living in the households of these individuals.
xiii. Current wearer of the test contact lens, MyDay® Multifocal.

5.4 Premature Withdrawal

A participant will be withdrawn from the investigation before completion if:

i. The participant withdraws his/her consent to be included in the trial;
ii. An adverse event takes place that is considered by the participant or the investigator to warrant withdrawal;
iii. Any event that leads the investigator to believe that it is not in the best interest for the participant to continue in the study;

iv. The study is prematurely terminated by the principal investigator, local research ethics committee or the Sponsor;
v. The participant is lost to follow-up;
vi. The participant no longer meets the eligibility criteria;
vii. The participant dies.

5.5 Informed Consent

Each participant will give written consent according to local requirements after the nature of the study has been fully explained. Informed consent will be obtained by a delegated investigator that is GCP trained. The consent form will be signed before performance of any study-related activity. The consent form will have received approval by both the Sponsor and by the reviewing IEC before its use. The informed consent will be in accordance with principles that originated in the Declaration of Helsinki, current ICH and GCP guidelines, applicable regulatory requirements, and sponsor policy. Should a participant indicate on their consent form that they would like their GP to be notified of their participation in the research, then a letter will be sent to the GP.

Before entry into the study, the investigator or an authorised member of the investigational staff will explain to potential participant the aims, methods, reasonably anticipated benefits, and potential hazards of the study, and any discomfort it may entail. The potential participant will be informed that his/her participation is voluntary and that he/she may withdraw consent to participate at any time. The participant will be informed that choosing not to participate will not affect the care the participant will receive. Finally, the potential participant will be told that if needed his/her records may be accessed by health authorities and authorized sponsor staff without violating his/her confidentiality, to the extent permitted by the applicable law(s) or regulations.

The participant will be given sufficient time to read the participant information sheet and the informed consent form [redacted] and will have the opportunity to ask questions. If he/she requires additional time, the participant will be able to sign the consent on a future date and the enrolment visit will be re-scheduled accordingly; no research related measurement will be carried out before the potential participant has signed the informed consent.

After this explanation and before entry into the study, consent will be appropriately recorded by means of the participants' dated signature and counter signature of the member of the research team taking consent of two originals. After having obtained the consent, a copy of the participant information sheet and of the signed informed consent form will be given to the participant; the other signed copy of the informed consent will be kept in the study file.

6 STUDY DESIGN & PROCEDURES

6.1 Experimental Design

The study will be conducted following an interventional, prospective, open label, sequential study design.

The design has been developed to represent the clinical situation to be tested, that is the refitting of successful Biofinity® multifocal contact lens wearers with MyDay® multifocal contact lenses as per the following routine:

i. Participants will be first fitted with Biofinity® multifocal contact lenses which they will wear for two weeks on a daily disposable wearing modality;
ii. At the completion of the two weeks of wear the participants will be refitted with MyDay® multifocal contact lenses that they will wear for two weeks on a daily disposable wearing modality.

The participants will attend the clinic for three study visits. The participants will not take part in any concomitant investigation of any type or take concomitant medications not allowed by the exclusion criteria.

6.2 Experimental Routine

Visit 1 – Screening /Enrolment / Fitting & Dispensing Biofinity® Multifocal Contact Lens

A prospective participant will attend the clinic for the first visit to initially obtain informed consent and evaluate the suitability to take part in the investigation. The potential participant will be asked to attend the clinic wearing spectacles and not have worn contact lenses that day. After informed consent has been given, the investigator will review the participant's medical history, ocular history [redacted] demographics and habitual contact lens wear history. A series of routine optometric assessments and tests will be conducted to determine the participant's prescription and evaluate the participant's ocular health.

Once it has been verified that the prospective participant meets the inclusion/exclusion criteria Biofinity® multifocal contact lenses will be inserted and worn for 10 minutes at which time the contact lens fit and vision will be assessed; [redacted]. If this is not achieved the participant will be discharged from the study; however, if a suitable fit is achieved the participant will then be instructed in the use of the contact lenses which will be dispensed to wear until Visit 2 as the main vision correction, aiming for at least 8 hours of wear a day for at least 5 days a week.

Visit 2 – Biofinity® Multifocal Contact Lens Follow-up & MyDay® Multifocal Contact Lens Fitting and Dispensing visit (14 ± 3 days after visit 1)

The participant will return for the second study visit after having worn the first study contact lenses for 14 ± 3 days. The participant will attend the visit wearing Biofinity® multifocal contact lenses, having worn the contact lenses for a minimum of three hours prior to the appointment.

The participant's medical, ocular, contact lens wearing history and concomitant treatments will once again be reviewed. [redacted]

At the completion of the ocular integrity check the MyDay® Multifocal contact lenses will be inserted and worn for 10 minutes at which time the contact lens fit and vision will be assessed; [redacted]. If this is not achieved the participant will be discharged from the study; however, if a suitable fit is achieved the participant will then will be instructed in the use of the contact lenses which will be dispensed to wear until Visit 3 as the main vision correction, aiming for at least 8 hours of wear a day for at least 5 days a week.

Visit 3 –MyDay® Multifocal Contact Lens Follow-up & Discharge Visit (14 ± 3 days after Visit 2).

The participant will return for the third study visit after having worn the second study contact lenses for 14 ± 3 days. The participant will attend the visit wearing MyDay® multifocal contact lenses contact lenses, having worn the contact lenses for a minimum of three hours prior to the appointment.

The participant's medical, ocular, contact lens wearing history and concomitant treatments will once again be reviewed. [redacted] Then the MyDay® Multifocal contact lenses contact lenses will be removed.

[redacted] the participant will be discharged from the study.

6.3 End of Study

The end of the study clinical phase is at the discharge of the last participant from the study. The overall completion of the study is when the clinical study reports, EC report and ISCRTN result posting have been completed.

6.4 Participant Instruction

The participant will be instructed to wear the study contact lenses daily for 14 ± 3 days, remove the contact lenses at night (prior to sleep), discard them and use a new identical pair of contact lenses the following day.

The participant will be advised on normal or adaptive symptoms related to contact lens wear. [redacted] These are not reported as adverse events unless in the investigator's opinion they are unexpected in nature, severity or have a high rate of occurrence.

[redacted]

The participant will be instructed to follow standard recommendations provided to contact lens wearers:

i. Avoid rubbing the eyes, always wash hands prior to touching the eyes or handling the contact lenses, avoid being in a dusty environment and to use sunglasses when outdoors.
ii. Exercise care while washing the face with tap water; avoid splashing tap water into the eyes.
iii. Do not swim with contact lenses whenever possible.
iv. Immediately contact the investigator and schedule to return to clinic for a check-up within 24 hours if the eyes become red, irritated or painful.

The participant will be provided with instruction sheets [redacted]

A participant using re-wetting eyedrops in combination with his/her habitual contact lenses will be able to continue to do so during the study.

6.5 Procedures

6.5.1 EFFICACY PROCEDURES

The primary efficacy procedures will be the rating of contact lens handling combining ease of insertion and ease of removal both recorded on 100-point visual analog scales.

The secondary efficacy procedure will be the measurement of high luminance [redacted] high contrast (> 90%) logMAR visual acuity at distance [redacted], intermediate [redacted] and near [redacted] using OTG-i Vision Suite.

[redacted]

[redacted]

[redacted]

i. [redacted]
[redacted]
[redacted]
[redacted].

6.5.3 POPULATION PROFILING PROCEDURES

The procedures to profile the population key characteristics will be:

i. Demographics and Medical & Ocular History [redacted]
ii. Habitual contact lenses wearing characteristics;
iii. [redacted]

6.5.4 STUDY MANAGEMENT PROCEDURES

The procedures to ensure that the study protocol is followed will be:

i. Contact lens fitting as per the Biofinity® multifocal contact lens fitting manual;
ii. Contact lens fitting as per the MyDay® multifocal contact lens fitting manual;
iii. Contact lens fit clinical classification;
iv. Recording of contact lens prescribing time;
v. Recording of number of contact lenses to arrive to the prescription to dispense;

6.6 Study Visit Routine

6.6.1 VISIT 1 – SCREENING ENROLMENT FITTING DISPENSING VISIT

The routine below will be followed:

- Explanation of the study[1]
- Signing of the consent form
- Participant demographics and ocular history questionnaire
- [redacted]
- [redacted]
- [redacted]
- Standard distance visual acuity [redacted]
- [redacted]
- Review of inclusion and exclusion criteria
- Decision to continue with determination of eligibility
- BIOFINITY® MULTIFOCAL INITIAL CONTACT LENS INSERTION AND WEAR FOR 10 MINUTES[4]
- [redacted]
- [redacted]
- [redacted]
- Study contact lens prescription suitability evaluation & decision to dispense or change contact lens power[3]

[redacted]

[redacted]

[redacted]

- BIOFINITY® MULTIFOCAL REMOVE INITIAL CONTACT LENS & INSERT BIOFINITY® MULTIFOCAL SECOND CONTACT LENS AND WEAR FOR 10 MINUTES[4]
- [redacted]
- [redacted]
- Standard distance, intermediate and near visual acuity with contact lenses (monocular & binocular)
- [redacted]
- Instruction for use
- Study product dispensing
- Scheduling

6.6.2 VISIT 2 – BIOFINITY® MULTIFOCAL CONTACT LENS FOLLOW-UP & MYDAY® MULTIFOCAL CONTACT LENS FITTING AND DISPENSING VISIT (14 ± 3 DAYS AFTER VISIT 1)

The routine below will be followed:

- [redacted]
- [redacted]
- [redacted]
- [redacted]
- LogMAR visual acuity measurement at distance, intermediate and near (monocular and binocular)
- BIOFINITY® MULTIFOCAL CONTACT LENS REMOVAL
- [redacted]
- Standard distance visual acuity [redacted]
- MYDAY® MULTIFOCAL INITIAL CONTACT LENS INSERTION AND WEAR FOR 10 MINUTES[7,8]
- [redacted]
- [redacted]
- Standard distance, intermediate and near visual acuity with contact lenses (monocular & binocular)
- Study contact lens prescription suitability evaluation & decision to dispense or change contact lens power[9]
- MYDAY® MULTIFOCAL REMOVE INITIAL CONTACT LENS & INSERT MYDAY® MULTIFOCAL SECOND CONTACT LENS AND WEAR FOR 10 MINUTES[9]
- [redacted]
- [redacted]
- Standard distance and near visual acuity with contact lenses (monocular & binocular)
- Study contact lens prescription suitability evaluation & decision to dispense or change contact lens power[10]
- Instruction for use
- Study product dispensing
- Scheduling

[4] [redacted]

6.6.3 VISIT 3– MYDAY® MULTIFOCAL CONTACT LENS FOLLOW-UP & DISCHARGE VISIT (14 ± 3 DAYS AFTER VISIT 2)

The routine below will be followed:

- [redacted]
- [redacted]
- [redacted]
- [redacted]
- [redacted]
- LogMAR visual acuity measurement at distance, intermediate and near (monocular and binocular)
- MYDAY® MULTIFOCAL® CONTACT LENS REMOVAL
- Safety ocular integrity[11]
- Standard distance visual acuity [redacted]
- Discharge

7 SAMPLE SIZE DETERMINATION AND STATISTICAL ANALYSIS

7.1 Sample Size Determination

Sample size calculations took into consideration that the two co-primary endpoints to assess contact lens handling, inserting and removal, will be both required to be met at the completion of the study to demonstrate the study hypothesis. Accordingly non-inferiority testing was carried out considering a power of 90% in order to achieve a final power of 80% to test simultaneously the two primary endpoints. No adjustment is required for α.

The results of a previous study involving similar population which measured contact lens handling (0-100 points visual analogue scale) achieved a standard deviation of the difference between two study contact lenses of 9.6 and 14.7 for insertion and removal respectively [1]. To demonstrate non-inferiority at both insertion and removal , considering a margin of non-inferiority of -7.00 and assuming no difference between test and control, for a one-sided paired t-test with α = 2.5% and ß = 10%, 49 participants are required to complete the study as per the protocol.

The reference study being conducted in the USA and involving a slightly different protocol (masked vs. open label) and considering that to be representative of the full range of presbyopes with similar number of young emergent, established and older advanced presbyopes with possible different levels of dexterity, the aim is to achieve a per protocol total population of 60 participants made up of approximately 20 in each of emergent low addition presbyopes (near addition +0.75D to +1.25D),established medium addition presbyopes (near addition +1.50D and +1.75D) and advanced high addition presbyopes (near addition+2.00D to +2.50D).

7.2 Statistical Analysis Plan

For all the key parameters recorded, summary tables including descriptive and/or distribution statistics will be given. For continuous and ordinal variables, the following descriptive statistics will be reported: mean, median, standard deviation, minimum, maximum, quartiles and sample size. For ordinal variables, and nominal variables distribution tables will be shown.

The comparison between test and reference contact lenses, in terms of ease of insertion (0-100 VAS) and ease of removal (0-100VAS) will be carried out using Generalized Linear Mixed Model. The model will include

[11] Eye rinse after ocular evaluation with fluorescein

contact lens (test, reference) and order (Visit1, Visit2) as fixed factor. Their interaction will be included in the analysis. The covariance structure that best models the residuals errors will be selected according to the AIC_C. The comparison between test and reference contact lens will be carried out using the 95% confidence interval (CI) of the mean difference estimated by GLMM. Non-inferiority will be demonstrated if the 2-sided 95% CI of the mean difference lies entirely above the margin of non-inferiority of -7.0. In the event that non-inferiority is demonstrated testing for equivalence will be carried out.

A detailed statistical analysis plan will be developed prior to database closure.

8 RISK ANALYSIS

8.1 Benefits

There might not be direct benefits to the participants in this study. However, participation in a study may contribute to scientific research information that may be used to optimise the refitting procedure of multifocal contact lenses. In addition, participants, who all have presbyopia and are current multifocal contact lens wearers, will have the opportunity to try the two contact lens vision alternatives, at no cost to them and identify if they prefer one type vs. the other and / or prefer either type to their own contact lenses. Any participant that prefers one of the two contact lens types to their own and wishes to switch contact lens type will be able to purchase the preferred contact lenses from their own eyecare practitioner at the end of the study.

8.2 Risks

All the assessments are routine clinical procedures or more detailed procedures, none presenting any increased risk to participants compared with normal clinical routine.

All participants will be current soft contact lens wearers. The risks of taking part in the study are no greater than those associated with wearing their own contact lenses. The reference and the test contact lenses are CE marked, currently marketed daily disposable contact lenses. The risks associated with wearing the reference and the test contact lenses are similar to wearing any type of approved marketed soft contact lens.

Complications may occur due to non-compliant behaviour. This will be mitigated by the investigator providing the participant with indications for use for the contact lenses prior to dispensing. The participants will be under the care of the research investigators for the four weeks study period and the investigators will be present to deal with any unexpected event.

The participants will have their vision checked at the onset of the study and prior to exiting the study to ensure that their vision remained unchanged.

8.3 Conclusion

OCULAR TECHNOLOGY GROUP - International has determined that the proposed clinical investigation, based on the users and products effectiveness risks and the risk management strategy in place (preventative and corrective), given that the severity of problems will be mostly minor, non-permanent and the likelihood of occurrence is unlikely with likelihood of non-detection if problem occurs being low, this study is justified as the overall potential benefit to the population outweighs its risks.

9 ADVERSE EVENTS AND REPORTING

9.1 Adverse Events

Adverse events including serious adverse events and quality complaints will be reported in accordance with ICH E6 Guideline for Good Clinical Practice. Adverse event reports to the Independent Ethics Committee and MHRA will be made according to their requirements.

9.1.1 ADVERSE EVENT DEFINITIONS

An 'adverse event' refers to any undesirable clinical occurrence in a participant, whether it is considered to be device-related or not.

Disease signs and symptoms present prior to the study product being utilised are not considered AEs, unless the condition re-appears or worsens in intensity or frequency during the study.

Adverse events (AE) may be classified as 'unanticipated adverse device effects,' 'serious adverse events,' 'significant adverse events,' or 'non-significant adverse events,' as defined below.

Classification	Definition
Serious Adverse Event (SAE)	A SAE is defined in accordance with ISO 14155 as an AE that: a. Led to death b. Led to serious deterioration in the health of the participant, that either resulted in 1. A life-threatening illness or injury, or 2. A permanent impairment of a body structure or a body function, or 3. Inpatient or prolonged hospitalization, or 4. Medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to a body structure or a body function, c. Led to foetal distress, foetal death or a congenital abnormality or birth defect NOTE: Planned hospitalization for a pre-existing condition, or a procedure required by the protocol, without serious deterioration in health, is not considered an SAE.
Adverse device effect (ADE)	An adverse device effect (ADE) is defined in accordance with ISO 14155 as "an adverse event related to the use of an investigational medical device." This definition includes any AEs resulting from insufficient or inadequate instructions for use, deployment, implantation, installation, or operation, or any malfunction of the investigational medical device as well as any event resulting from use error (per ISO 62366) or from intentional misuse of the investigational medical device.
Unanticipated Adverse Device Effect (UADE)	An unanticipated adverse device effect (UADE) is defined in accordance with 21 Code of Federal Regulations (CFR) 812.3 as "any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects."
Serious adverse device effect (SADE)	A serious adverse device effect (SADE) is defined in accordance with ISO 14155 as "an adverse device effect that has resulted in any of the consequences characteristic of a serious adverse event."

AE classification, coding (for reporting to the sponsor) and examples are provided in the following table of Contact Lens Adverse Event Classification and Reporting table:

Code	Condition	Potential AE Classification	Reporting
01	Presumed infectious keratitis or infectious corneal ulcer	SERIOUS	

02	Permanent loss of ≥ 2 lines of best spectacle corrected visual acuity (BSCVA)	SERIOUS	Notify sponsor as soon as possible, **within 24 hrs;** Independent Ethics Committee reporting as per requirements
03	Corneal injury that results in permanent opacification within central cornea (6mm)	SERIOUS	
04	Uveitis or Iritis (e.g. presence of anterior segment inflammation as described in ISO 11980, Annex B)	SERIOUS	
05	Endophthalmitis	SERIOUS	
06	Hyphema	SERIOUS	
07	Hypopyon	SERIOUS	
08	Neovascularization within the central 6mm of cornea	SERIOUS	
00	Other serious event	SERIOUS	
11	Peripheral (outside central 6mm), non-progressive, non-infectious ulcer	SIGNIFICANT	Notify sponsor as soon as possible, **within 5 working days**; Independent Ethics Committee reporting as per requirements
12	Symptomatic corneal infiltrative event	SIGNIFICANT	
13	Superior epithelial arcuate lesions (SEALs) involving epithelial split	SIGNIFICANT	
14	Corneal staining ≥ dense coalescent staining up to 2mm in diameter (e.g. moderate, ISO 11980 grade 3)	SIGNIFICANT	
15	Corneal neovascularization ≥ 1.0mm vessel penetration (e.g. ≥ ISO 111980 Grade 2), if 2 grade change from baseline	SIGNIFICANT	
16	Any temporary loss of ≥ 2 lines BSCVA for ≥ 2wks	SIGNIFICANT	
17	Any sign and/or symptom for which participant is administered therapeutic treatment or which necessitates discontinuation of contact lens wear for ≥ 2 weeks	SIGNIFICANT	
10	Other significant event	SIGNIFICANT	
21	Conjunctivitis (bacterial, viral or allergic)	NON-SIGNIFICANT	
22	Papillary conjunctivitis if ≥ mild scattered papillae/follicles approximately 1mm in diameter (e.g. ISO 11890 Grade 2), if 2 grade change from baseline	NON-SIGNIFICANT	
23	Asymptomatic corneal infiltrative events	NON-SIGNIFICANT	
24	Any sign and/or symptom for which temporary contact lens discontinuation for > 1 day is recommended (if not already classified)	NON-SIGNIFICANT	
20	Other sign and/or symptom warranting classification as a non-significant adverse event	NON-SIGNIFICANT	

9.1.2 NORMAL OR ADAPTIVE SYMPTOMS

Transient symptoms such as end-of-day dryness, contact lens awareness, itching or burning or other discomfort may occur with contact lens wear and may occasionally reduce wearing time. These are not reported as adverse events unless in the investigators' opinion they are unexpected in nature, severe or have a high rate of occurrence.

This clinical study will also ascertain satisfaction or preference with participative attributes such as comfort, vision, or contact lens handling. Responses to these participative questionnaires will not be considered as adverse events, complaints or device malfunctions.

9.1.3 PROCEDURES FOR ADVERSE EVENTS

Treatment of an adverse event will depend on its nature and severity. Based on the clinical judgment of the investigator the participant may be referred to an ophthalmologist for treatment. The investigator will attempt

to determine whether the reaction is related to the contact lenses or a result of other factors. An Adverse Event Form will be completed for each adverse event. If both eyes are involved, each eye will be counted as one adverse event and Adverse Event information will be completed *for each eye*. Whenever possible, the adverse event will be photo documented.

Expenses incurred for medical treatment as part of study participation will be paid by the sponsor (bills and prescription receipts kept). The participant must be followed until resolution and a written report completed indicating the subsequent treatment and resolution of the condition.

9.2 Reporting Adverse Events

All potential Serious and Unanticipated Adverse Device Effects that are related or possibly related to participation will be reported to the Principal Investigator and the sponsor within 24 hours of the investigator becoming aware of the event. The Principal Investigator will report the event to the Ethics Committee as soon as possible (by fax, mail/delivery, phone, or email) following the site Independent Ethics Committee guidelines. All fatal or life-threatening events will be reported immediately to the Independent Ethics Committee.

Significant and Non-Significant Adverse Events will be reported to the sponsor using the Adverse Event notification form as soon as possible, but no later than 5 working days after the occurrence.

Sponsor contact details are:

[redacted]

10 DEVICE DEFICIENCIES

Device deficiencies are defined as inadequacy of a medical device with respect to its identity, quality, durability, reliability, safety or performance. For contact lens products “Product Defect” is the terminology typically used for an *unexpected* observation related to the identity, quality, durability, reliability, or usability of the product under investigation.

NOTE: Observations on study products that are anticipated as a part of the device development process are not considered to be Product Defects or Device Deficiencies.

Product Defects or Device Deficiencies reporting depends upon its severity and association with any concurrent adverse event as follows:

i. If the Product Defect is associated with an adverse event, the investigator shall report the Product defect via the Adverse Event Notification Form.
ii. If the Product Defect is not associated with an adverse event, the investigator shall report the Product Defect via the Clinical Product Defect Notification Form.
iii. If the investigator judges that the Product Defect could have led to a Serious Adverse Event if no preventative action was taken, the Product Defect should be reported to the Sponsor via the Product Defect Notification t Form within 24 hours of becoming aware of the defect. The investigator should report to the IRB/EC per their reporting requirements.
iv. All other Product Defects should be reported to Sponsor as soon as possible, but no later than 5 working days after occurrence.

Sponsor contact details for Product Defect Notifications are:

[redacted]

11 INVESTIGATOR, SPONSOR AND MEDICAL MONITOR RESPONSIBILITIES

11.1 Investigator Responsibilities

The investigator is responsible for ensuring participant safety and data quality by: protocol compliance, adherence to GCP and local regulatory requirements, and the Declaration of Helsinki. The investigator should be appropriately qualified and legally entitled to practice and be trained in the proper method of obtaining informed consent.

The investigator must have the appropriate resources to conduct the clinical trial, be familiar with the protocol and agree to adhere to it, support monitoring and auditing activities, communicate with the Sponsor regarding any clinical trial issues or need for protocol modifications, make the necessary arrangements to ensure proper conduct and completion of the clinical trial, and ensure the protection and welfare of the participant, including arranging any emergency treatment as needed.

The investigator must ensure written Ethics Committee approval is received prior to the start of the clinical trial, that the Ethics Committee and sponsor is kept informed of the clinical trial progress, including serious/adverse events and deviations as required by them, and that any changes to the protocol are notified to the Ethics Committee and review written approval prior to implementation.

The investigator must try to ensure adequate participant recruitment; that all necessary and appropriate information is given to potential participants and consent is taken and that documents and clinical records indicate the participant is enrolled in a clinical trial.

The investigator has primary responsibility for the accuracy, legibility and security of all clinical investigation data, video recordings, documents and participant records at the Investigator site during and after the clinical trial. CRFs are to be signed by the investigator, and any alterations to data are to be made by authorised personnel, initialled and dated by same or, in the instance of electronic data, an audit trail will be in place, with no obstruction of the original data.

The investigator must ensure that data be kept for the minimum time as specified by this protocol. The study product must be accounted for (the quantity of the devices received must be reconciled with the quantities of the device used, discarded or returned), and must also be responsible for the supervision and assignment of duties to all responsible for the conduct and evaluation of the clinical trial for the Investigator centre involved

11.2 Sponsor Responsibilities

The Sponsor has delegated the selection of the Investigator and study site to the CRO, who should also select and appoint a monitor. The Sponsor has the ultimate responsibility for monitoring. The Sponsor is to supply and keep an up-to-date signed protocol and protocol amendments.

The sponsor should ensure appropriate information is provided to the Investigators to conduct the clinical trial; that deviations are reviewed with the Investigator as needed and included in the final report. Adverse events are reported by the investigator, and the sponsor in turn will then notify their applicable regulatory authorities, and other investigators as appropriate. Product Defect reporting are reported by the investigator and shall be report via the Clinical Product Defect Notification Form and will be included in the final report.

The Sponsor is to maintain Sponsor-specific clinical trial documentation as required by the regulatory authorities and to ensure the investigator is aware of their record keeping responsibilities.

11.3 Medical Monitor Responsibilities

The Medical Monitor will be a medical practitioner specialising in ophthalmology. To reduce study bias concerns, the Medical Monitor will not have any real or potential conflict of interest with the Sponsor, Study Investigator or participating Investigative site.

The primary purpose of the Medical Monitor is to ensure an independent review all Serious Adverse Events (SAE), device-related Adverse Events and AE related to the safety endpoints. When reviewing SAE and device-related adverse events, the Medical Monitor will report the relationship between the AE and the study device and the study procedure. The results of all events reviewed by the Medical Monitor will be documented.

The Medical Monitor for the OTG-i Research Clinic will be [redacted] contracted to OTG-i Research Clinic for this activity.

12 GENERAL CLINICAL MANAGEMENT

12.1 Data Recording

The clinical data will be recorded on dedicated electronic case report forms (eCRFs) specifically designed to match the testing routine for each visit. [redacted] All data captured with this software will be stored in a secure SQL database. The eCRFs will be reviewed for accuracy and comprehensiveness once completed and signed by the investigator. A summary of the data will also be recorded in the participants' clinical records. These constitute the participants' source documents, which will be signed by the investigator. The content and structure of the eCRFs are compliant with ISO14155:2011.

12.2 Clinical Monitoring

OCULAR TECHNOLOGY GROUP - International will monitor the study in a manner consistent with ICH GCP E6, ENISO14155:2020 and the Declaration of Helsinki. The study monitor will maintain close contact with the Principal Investigator and the Investigator's designated staff. The monitor's responsibilities will include:

i. Ensuring that the investigation is being conducted according to the protocol;
ii. Ensuring the rights and wellbeing of participants are protected;
iii. Ensuring that protocol deviations are documented with corrective action plans, as applicable;
iv. Clarifying questions regarding the study;
v. Resolving study issues or problems that may arise;
vi. Reviewing the study records to ensure completeness and accuracy;
vii. Study and participant source document records reviewed will include:
    a. The Information and Consent Form
    b. Source documentation including consenting, medical history, concomitant medications and adverse event information as applicable.
    c. Study related Regulatory documents as per ICH E3 section 8

The clinical monitor will review study data and will perform, at a minimum, one Interim and one Close-Out Visit on site.

12.3 Study Product Accounting

Study product records include the study contact lens shipping orders, dispensing logs and the physical count and disposition of the remaining unused study contact lenses. Used worn contact lenses collected at the study visits will be discarded by the study site personnel. The clinical monitor will ensure product is reconciled and any discrepancies are investigated and either corrected or documented. At study conclusion all study contact lenses will be reconciled.

12.4 Participant Compliance Monitoring

Throughout the course of the study the clinical monitor will review study data for participant compliance to the protocol. Non-compliances will be documented as protocol deviation(s). If a deviation is determined to be major, the deviation will be reported to the Ethics Committee as per their requirements.

13 ADMINISTRATIVE MANAGEMENT

13.1 Relevant Standards

This clinical study will be conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki, and in compliance with the International Conference on Harmonization (ICH) E6 Good Clinical Practice (GCP) Consolidated Guideline, the International Standards Organization (ISO) Clinical investigation of medical devices for human participants – Good clinical practice (ISO 14155:2020(E)), Ophthalmic optics – Contact lenses and contact lens care products – Guidance for clinical investigations (ISO 19980:2012 (E)) and other regulations as applicable. The Investigator and all clinical study staff will conduct the clinical study in compliance with the protocol. The Investigator will ensure that all personnel involved in the conduct of the study are qualified to perform their assigned responsibilities through relevant education, training, and experience.

13.2 Deviations from the Protocol

13.2.1 GENERAL

Protocol deviations are unanticipated or unintentional changes to a study after it has received prior sponsor approval and ethics clearance. Protocol deviations can be major or minor.

If the deviation affects participant's rights, safety and wellbeing, or the scientific integrity of the clinical investigation, the ethics committee must be contacted with requests for deviations, and reports of deviations. Under emergency circumstances, deviations from the clinical investigational plan to protect the rights, safety and well-being of participants may proceed without prior approval of the sponsor and the ethics committee. Such deviations shall be documented and reported to the sponsor and the ethics committee as soon as possible.

13.2.2 MAJOR PROTOCOL DEVIATIONS

Major protocol deviations may impact the research protocol, information consent document or other study materials, usually cannot be anticipated ahead of time and are often necessary to ensure the safety and welfare of the participants.
The following are examples of protocol deviations that must be reported to the EC and MHRA:

i. Changes in procedures initiated to eliminate immediate risks/hazards to participants;
ii. Enrolment of participants outside the protocol inclusion/exclusion criteria whether agreed to or not by the sponsor;
iii. Inadvertent deviation in specific research intervention procedures or timing of the research intervention which could impact upon the safety or efficacy of the study-related intervention or upon the experimental design;
iv. Information consent documentation violations: no documentation of informed consent; incorrect version of, or incomplete, informed consent documentation used.

13.2.3 MINOR PROTOCOL DEVIATIONS

Protocol deviations caused by or which originate with research participants are generally considered minor, and normally are not reported to the Independent Ethics Committee unless these result in increased risk to the participants). The following are examples of protocol deviations that are considered minor and do not require reporting to the Independent Ethics Committee and MHRA:

i. Logistical or administrative aspects of the study (e.g., study participant missed appointment, change in appointment date);
ii. Inadvertent deviation in specific research intervention procedures or timing of the research intervention which would *not* impact upon the safety or efficacy of the study-related intervention or upon the experimental design (i.e., missing a measurement during a session that is not considered critical for the study).

13.3 Modifications to the Clinical Investigational Plan

Any modifications to the clinical investigational plan that are considered necessary can only be effected after approval from the principal investigator and the Independent Ethics Committee. In an emergency situation, as indicated in ISO14155, the clinical investigator will exercise his judgement to safeguard the participant's interest and may deviate from the clinical investigation plan without the prior approval of the Independent Ethics Committee. In that case, the deviation will not be considered as a breach of agreement but will be reported to the ethics committee.

13.4 Termination of the Study

The Sponsors reserve the right to terminate the study at any time for any reason. The principal investigator has the discretion to initiate stopping the study based on participant safety or if information indicates the study's results may be compromised. The Investigator should promptly notify the IEC of the termination or suspension and of the study and the reason.

13.5 Data Protection

All information obtained during the course of the investigation will be regarded as confidential and will be handled in accordance with the Data Protection Act and the General Data Protection Regulation (GDPR) guidelines. All personal data gathered in this trial will be treated in strictest confidence by investigators, monitors, OTG-*i* personnel, the sponsor and the independent ethics committee. No data will be disclosed to any third party without the express permission of the participant concerned, with the exception of OTG-*i* personnel (monitor, auditor), the sponsor, the independent ethics committees and regulatory organisations in the context of their investigation related activities which, as part of the investigation will have access to the CRFs and source documents.

13.6 Data Handling and Record Keeping

The data analysis will be carried out by OTG-*i*.

All records, including CRFs, will be kept in the files of the Principal Investigator site for the latter of the two dates a period of two years after the date on which the investigation is terminated or completed, or the date that the records are no longer required for legal clinical requirements.

13.7 Reporting

OTG-*i* shall submit a final report to the sponsor as per the terms in the Statement of Work.

OTG-*i* shall also submit a summary one-year update and/or a summary final report to the Independent Ethics Committee.

13.8 Publication Policy

The study data will be wholly owned by the Sponsor. The results of the study may <u>not</u> be used in publications or presentations without the written permission of the Sponsor.

[redacted]

[redacted]

13.10 Indemnity / Insurance

The Sponsor will take out indemnity to cover the participants and research staff involved in the study and the ethics committee. This will NOT cover the research staff for clinical negligence. Investigators will have their own professional indemnity

[redacted]

[redacted]

[redacted]